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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/852,547	05/10/2001	David A. Sirbasku	057041-000004	6474

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111 MONUMENT CIRCLE, SUITE 3700
INDIANAPOLIS, IN 46204-5137

EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1643	

NOTIFICATION DATE	DELIVERY MODE
03/05/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DocketDept@uspatent.com

Office Action Summary	Application No.	Applicant(s)	
	09/852,547	SIRBASKU	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *95-109* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *95-104* is/are rejected.

7)☒ Claim(s) *105-109* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 95-101 have been amended. Claims 95-109 are pending and under consideration.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 95-104 are rejected under 35 U.S.C. 103(a) as being unpatentable over Furuya et al (Cancer Research, December 1989, Vol. 49, pp. 6670-6674) in view of Hoffman ('The Biochemistry of Clinical Medicine', 1970, pages 48 and 55).

Claim 95 is drawn to a method to quantitate immunoglobulin steroid hormone response inhibitor in a sample comprising:

treating a sample to effectively remove steroid hormones from said sample;

adding the treated sample to a first group of steroid hormone responsive tumor cells which have been transferred to serum-free media which have been transferred to serum, free media, said cells selected from a group consisting of T47D, MCF-7A, MCF-7K, ZR-75-1; MTW9/PL2; GH3. GH1: GH4Cl or H-301;

adding a known amount of plasma immunoglobulin selected from a group consisting of plasma IgA, plasma IgM to a second group of said steroid hormone responsive tumor cells which have been transferred to serum-free media which have been transferred to serum, free media;

determining an amount of the added treated sample at which said treated sample inhibits steroid hormone mediated cell growth in said inhibitor assay;

comparing said amount of added treated sample to said amount of plasma immunoglobulin added to quantitate an amount of immunoglobulin steroid hormone response inhibitor in said treated sample.

Claim 96 is drawn to a method of detecting inhibition of steroid hormone responsive cell growth wherein the inhibition can be reversed by steroid hormone comprising

obtaining at least two sample of identical mucosal epithelial cultured cells

treating one of said cell samples with purified polymeric IgM;

leave one sample without purified polymeric IgM

incubating said cell samples under growth promoting conditions

measuring post-incubation, cell population doublings, and

detecting inhibition of steroid hormone responsive cell growth from decreased cell population doublings in the cell sample treated with purified IgM compared with the sample left untreated.

Claim 97 is drawn to a method of detecting inhibition of steroid hormone responsive cell growth wherein the inhibition can be reversed by steroid hormone comprising

obtaining at least two sample of identical mucosal epithelial cultured cells

treating one of said cell samples with purified is drawn to a method of detecting inhibition of steroid hormone responsive cell growth wherein the inhibition can be reversed by steroid hormone comprising

obtaining at least two sample of identical mucosal epithelial cultured cells

treating one of said cell samples with purified plasma IgA;

leave one sample without purified plasma IgA

incubating said cell samples under growth promoting conditions

measuring post-incubation, cell population doublings, and

detecting inhibition of steroid hormone responsive cell growth from a decreased cell population doublings in the cell sample treated with purified plasma IgA compared with the sample left untreated.

Claim 98 is drawn to a method of detecting estrogenic activity of a substance of interest comprising

adding an inhibitory amount of purified IgM to at least two samples of a steroid hormone responsive cancer cell population maintained in nutrient medium

making a test mixture by adding an amount of the substance of interest to one of the samples

incubating the cell samples including untreated cells for a period of time under growth promoting conditions

measuring the cell population doubling in the cell samples after a period of time, and

detecting estrogenic activity of the substance of interest from increased cell population doublings in the treated sample relative to the untreated sample.

Claim 99 is drawn to a method of detecting estrogenic activity of a substance of interest comprising

adding an inhibitory amount of purified IgA to at least two samples of a steroid hormone responsive cancer cell population maintained in nutrient medium

making a test mixture by adding an amount of the substance of interest to one of the samples

incubating the cell samples including untreated cells for a period of time under growth promoting conditions

measuring the cell population doubling in the cell samples after a period of time, and

detecting estrogenic activity of the substance of interest from increased cell population doublings in the treated sample relative to the untreated sample.

Claim 100 is drawn to a method of detecting estrogenic activity of a substance of interest comprising

adding an inhibitory amount of purified IgM to at least three samples of a steroid hormone responsive cancer cell population maintained in nutrient medium.

adding an amount of a substance of interest to one of the cell samples to provide a test mixture;

adding an amount of estrogen to one of the cell samples to yield a standard mixture;

incubating the cell samples including untreated cells for a period of time under growth promoting conditions

measuring the cell population doubling in the cell samples after a period of time, and

detecting estrogenic activity of the substance of interest from a significant increased in cell population doublings in the test mixture relative to the untreated sample.

Claim 101 is drawn to a method of detecting estrogenic activity of a substance of interest comprising

adding an inhibitory amount of purified IgA to at least three samples of a steroid hormone responsive cancer cell population maintained in nutrient medium.

adding an amount of a substance of interest to one of the cell samples to provide a test mixture;

adding an amount of estrogen to one of the cell samples to yield a standard mixture;

incubating the cell samples including untreated cells for a period of time under growth promoting conditions

measuring the cell population doubling in the cell samples after a period of time, and

detecting estrogenic activity of the substance of interest from a significant increased in cell population doublings in the test mixture relative to the untreated sample.

Claim 102 embodies the method of claim 95 wherein said cells are selected from T47D, MCF-7A, MCF-7K, or ZR-75-1. Claim 103 embodies the method of claim 102 wherein said cells are from the T47D cell line. Claim 104 embodies the method of claim 102 wherein said cells are from the Z R-75-1 cell line

Furuya et al teach that estradiol can neutralize growth inhibition exerted by the ammonium sulfate treated fraction of bovine serum. Furuya et al teach that bovine serum albumin fraction V containing globulin remnants inhibited cell growth, but that globulin-free bovine serum albumin did not inhibit cell growth (abstract). One of skill in the art would reasonably conclude that serum globulins were potentially the cause of the growth inhibition which estradiol, at sufficiently high concentrations, could overcome. Furuya et al teach that the established human breast cancer cell lines of MCF-7, ZR-75-1 and T47D (page 6670, lines 1-5 under "Introduction"). Furuya et al teach the attempt to study specific growth inhibiting characteristics of a standard , purified amount of a serum constituent as a putative serum-

inhibition factor and to determine the genuine effects of exogenous estrogen and/or tamoxifen, including the dual effect of estrogen in the presence of the serum growth inhibitor and a direct mitogenic effect of estrogen, and the inhibition thereof by tamoxifen (page 6670, second column, first full paragraph). Furuya et al teach that low and high doses of tamoxifen exert estrogenic and antiestrogenic effects, respectively, on MCF-7 cells, and that growth inhibition by tamoxifen decreases with increasing concentration of sGF or DCFBS, relative to serum free AIT medium, which when combined with tamoxifen demonstrated a lethal effect on MCF-7 cells (page 6674, fist column). Furuya et al teach that the mechanism of said effect has not yet been elucidated. Furuya et al do not teach growth stimulation by estrogen in the presence of the serum inhibitor which is purified plasma IgA, or purified plasma IgM.

Hoffman et al teach the constituents of serum include IgM, IgG and IgA within the globulin fraction (page 48, figure 4B). Hoffman et al teach that the globulin fraction of serum is ~2.5 g/100 ml of serum and albumin makes up the majority of the remainder of the protein content of serum (page 55, table 10, values for "Normal").

It would have been prima facie obvious to test the inhibitory contribution of various serum globulin proteins, such as IgM, IA or IgG in order t identify the growth inhibitory factor in serum, and the factor responsible for inhibiting the toxic activity of tamoxifen on the human breast cancer cell lines of MCF-7, ZR-75-1 and T47D. One of skill in the art would have been motivated to do so in order to understand the mechanisms and possible in vivo confounding factors effecting the action of drugs such as tamoxifen in vivo. It would have been further obvious to carry out the tests using various combinations of estrogen, tamoxifen and the putative serum inhibitory factors such as IgM, IgG or IgA in multiple samples in order to determine if a statistically significant variation between samples with differing constituents was occurring.

Claims 105-109 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

All other rejections and objections as set forth in he prior office action are withdrawn in light of applicant's amendments.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen A Canella/
Primary Examiner, Art Unit 1643